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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,925	09/15/2005	Raymond John Steptoe	18749	8585

272 7590 07/17/2007

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
07/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,925	STEPTOE ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-25 are pending and under current examination.

Claim Objections

Claim 1 is objected to because of an undefined acronym "APC".

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 10, 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Bochan et al* (Transplant proc 1999;31:690-1), in view of *Burt et al* (Autoimmunity Rev 2002;1:133-8).

Bochan et al teach a method for treating insulin-dependent diabetes in a subject comprising collecting a sample of hematopoetic stem cells from the bone marrow of the rat, infecting the HSCs with a recombinant AAV vector expressing rat proinsulin, and reintroducing the transfected HSCs to rats with STZ-induced diabetes. *Bochan et al* reported transgene expression in several tissues of the rat, and the expression lasted for up to 6 wks, and in the short term, they were able to reverse STZ-induced diabetes (e.g. figs and page 691).

Although *Bochan et al* do not specify whether the HSCs injected to STZ-diabetic rats are autologous, this is known in the art as taught by *Burt et al* (§ 4). Although *Bochan et al* conducted the experiment in rat, and used rat proinsulin II, it is clear the investigation was a feasibility study for treating diabetes in humans.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Bochan et al,* in treating human diabetes upon completion of necessary pre-clinical studies and use autologous HSCs and human insulin in a human subject, with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the ultimate goal of animal study is to develop a treatment strategy for treating human diabetes. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Bochan et al* (Transplant proc 1999;31:690-1), in view of *Burt et al* (Autoimmunity Rev 2002;1:133-8) as applied to claims 1-8, 10, 12-16 above, further in view of *Slavin et al* (USP 6428782).

Bochan et al in view of *Burt et al* as discussed *supra* do not detail that the HSCs undergo cytokine-mediated mobilization. *Slavin et al* supplemented the deficiency by establishing it was routine in the art to use cytokine-mediated mobilization to increase the numbers of HSCs extracted from bone marrow (e.g. detx16).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to mobilize HSCs in the method taught by *Bochan et al* in view of *Burt et al* in order to obtain sufficient numbers of HSCs for therapeutic use, with a reasonable expectation of success. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir.1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the scope of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

Claims are drawn to administering antigen-presenting cells expressing proinsulin or an immunogenic homolog of proinsulin for treating insulin-dependent, however, the specification fails to teach it is the proinsulin-induced immune response that asserted a therapeutic effect in a subject having insulin-dependent diabetes.

Turning to the state of the art, it was well known in the art that the underlying mechanism of autoimmune diabetes is associated with destruction of insulin-secreting beta cells of pancreas, and diabetes-prone NOD mice have increased dendritc cells that contribute to the onset of autoimmune diabetes

(*Steptoe et al*, J Immunol 2002;168:5032-41). In view of such, administering more dendritic cells expressing proinsulin would likely to induce or exacerbate autoimmune diabetes rather than treating it. In view of such, the invention does not appear to be enabled in the absence of clarification of the contradictory evidence found in the reference.

Claims 9, 17, and 25 recite a humanized proinsulin derived from non-human animals, however, the specification fails to teach what is the structure of the "humanized" proinsulin or how to make such, and thus, it fails to provide an enabling disclosure for what is now claimed.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 18-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-9 are vague and indefinite because claim 1 requires introducing into a subject in need a genetically modified APC, whereas the method step comprising administering HSCs or HPCs. It is unclear how introducing HSCs is associated with introducing APCs, and thus the metes and bounds of the claims are uncertain.

Claims 1-9 are vague and indefinite because a step is missing in claim 1, i.e. introducing the genetically modified HSCs back to the subject. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6.

Claims 18-25 provide for the use of a genetically modified APC, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 18-25 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 21 recites the limitation "said HSCs and/or HPCs". There is insufficient antecedent basis for this limitation in the claim.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
July 9, 2007